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V_2O_5 dust is good. It was originally suggested by Roschin[652] on the basis of animal studies of short duration, and its suitability was subsequently confirmed in more extensive animal studies by Stokinger *et al.*[633] Lewis[638] has more recently reported no toxic manifestations from V dusts among workmen exposed to from 0.1 to 0.3 mg. of V/cu. meter. The lower limit for V_2O_5 fume is based on the recognized greater toxicity of fume compared with dusts of larger particle size.

ZINC, Zn

STAT

1. *Source and Production*

Zn is widely distributed and occurs in small amounts in almost all igneous rocks. Sphalerite (zinc blende) ZnS is the principal Zn mineral. Depending on Fe content, natural specimens range in color from light tan to black; above a ratio of Fe:Zn of 1:5 the mineral is called marmatite; above 5:6 the sphalerite structure ceases to exist. Next to Fe, Cd is the most common impurity in sphalerite; when associated with Zn as CdS it is called greenochite. Cd is about $^1/_{200}$ as abundant as Zn. Ga and Ge also occur in sphalerite (low-temperature formation), Sn and In occur in traces from high-temperature deposits. Pb minerals are commonly associated with Zn minerals; the ratio Zn:Pb varies widely, from 1:7 to 5:1. Other commonly associated minerals are calcite ($CaCO_3$), dolomite ($CaCO_3 \cdot MgCO_3$), pyrite (FeS_2), quartz (SiO_2), chalcopyrite ($CuFeS_2$), and barite ($BaSO_4$). Other oxidized forms of Zn minerals, such as ZnO, $ZnSO_4 \cdot 7H_2O$, $ZnCO_3$, $Zn_4Si_2O_7(OH)_2 \cdot H_2O$, and $(Zn,Mn)O \cdot Fe_2O_3$, can be thought of as alterations from the sulfide, and are of minor importance.

United States mines produced 412,000 tons recoverable Zn in 1958, 23 per cent less than in 1957 and the smallest annual amount since 1933. Oversupply, increased world production, declining consumption, cessation of government stockpiling, and lower Zn prices contributed to lessened domestic production.

A variety of mining methods are used, which vary with the type of ore body. Underground methods yield most production but some open-pit mining is done. Almost all loading and transportation are handled by power, at present; electric or diesel units supply the power. Production of Zn concentrates is done by crushing and grinding followed by gravity separation, flotation, or magnetic methods, or combinations of them, depending on the complexity of the ore. Considerable metal loss occurs on concentrating; losses of 8 to 20 per cent occur with the sulfide and 15 to 90 per cent of the oxidized Zn. To improve recoveries of the latter, a caustic-leach electrolytic process is used; in this, Zn is extracted from the ores by NaOH solution, the resulting electrolyte is purified with Zn dust and lime, and the Zn is electrodeposited. Zn smelting refers to treatment whereby Zn ores or concentrates are reduced to refined metal. Sulfide Zn concentrates are roasted to eliminate S; in the process Zn is converted to the oxide and small amounts of $ZnSO_4$. The roast may either be leached for electrolytic deposition of Zn, or combined with coke or

[652] I. V. Roschin, *Gigiena i Sanit.*, 11, 49 (1952).

coal and retorted at about 1100°C. Residues from leaching and distillation are shipped to a lead smelter for further processing if they contain economic amounts of metals (Pb, Au, and Ag). Domestic smelters produce Zn of various grades; electrolytic plants produce special high-grade or high-grade slab Zn; slab Zn from horizontal retort plants is mostly prime western grade, although smaller amounts of other grades are produced; vertical retort plants produce regular high grade; all other grades are produced as the market warrants.

2. *Uses and Industrial Exposures*

Zn as metal in slab or pig was used to the extent of 868,300 tons in 1958; ore and concentrates for pigments and salts, 94,900 tons; as scrap for alloys, Zn dust pigments, and salts, 178,900 tons; other Zn concentrate is used for galvanizing, the largest single use (40 per cent of total slab production). Second largest use of slab Zn is in die-casting: as Zn alloy, of which parts as small as zipper elements or as large as automobile radiator grilles are made. The automobile industry uses a great number of Zn die-castings, as do the electric appliance, light machine, tool, hardware, and toy industries. Large quantities of Zn are used for brass, particularly in wartime for cartridges and shell cases, but developments in weapons and ammunition are lessening the need for Zn. Zn, in sheet and rolled forms as an alloy, is used in dry cells; jar caps (whence comes Cd in our diet); weather stripping; photoengraving plates; roofing; ship's hulls; pipelines; and heavy plates for cathodic protection of steam boilers. Zn pigments and salts, chief of which are ZnO, lithopone ($ZnS + BaSO_4$), $ZnCl_2$, and $ZnSO_4$, have innumerable uses; the major ones are in rubber goods, linoleum, paints, ceramics, cosmetics, textiles, paper filler, and pharmaceuticals. Leaded ZnO is used in paints, varnishes, coated fabrics, and textiles; $ZnCl_2$, for wood preservation, dry-battery cells, refining oil, soldering flux; $ZnSO_4$, in rayon, fertilizers, glue, textile dyes, electrogalvanizing solutions, economic poisons, pure chemicals, and soap. About 30,000 tons of Zn dust is used as a reducing agent in the synthesis of dye intermediates, of Na and Zn hydrosulfite, in metallic paints, and cladding of iron and steel products (sherardizing). Organic Zn compounds of the type R_2Zn have limited application in organic synthesis.

Industrial hazards arise from exposure to Zn fume, notorious producer of metal-fume fever, but associated hazards in the metallurgy of Zn, of more serious consequence, arise from the presence of As, Cd, Mn, Pb, and possibly Cu and Ag. The frequent presence of As in Zn is a source of exposure to arsine (AsH_3) whenever Zn is dissolved in acids or alkalies; many cases of intoxication by AsH_3 have occurred in the pickling of galvanized iron or from the use of powdered impure Zn as a reducing agent in dyeing. It is possible also that effects attributed to exposure to Zn fume may in part be attributable to those of Cd. Cd occurring uniformly as a contaminant in Zn is a continuous source of trace amounts of Cd in man.

3. *Physical and Chemical Properties*

The physical and chemical properties of Zn and some of its compounds are listed in Table 42.

TABLE 42

Physical and Chemical Properties of Zn and Some of Its Compounds

	Chemical symbol	At. or mol. wt.	Sp. gr.	M.p., °C.	B.p., °C.	Solubility
Zinc	Zn	65.38	7.14	419.47	907	Insol. hot or cold H_2O Sol. acids, alkalies, acetic acid
Zinc oxide	ZnO	81.38	5.47	>1800		1.6 mg./liter(29°) Sol. acids, dil. acetic acid, NH_4OH
Zinc sulfide (sphalerite)	ZnS	97.45	4.102(25°)	Tr. 1020		0.65 mg./liter(18°) V. sol. acids
Zinc chloride	$ZnCl_2$	136.29	2.91(25°)	262	732	4.32 kg./liter(25°) 6.15 kg./liter(100°) 1 kg./liter alc.(12.5°) V. sol. ether Insol. NH_3
Zinc sulfate	$ZnSO_4$	161.44	3.74(15°)	Dec. 740		865 g./liter(80°) 808 g./liter(100°) Sl. sol. alc.
Dimethyl zinc	$(CH_3)_2Zn$	95.45	1.386(10.5°)	−42.2	46	Dec. cold H_2O, alc., acids Sol. ether

Zn is a silvery metal of low to intermediate hardness; rolled Zn, 99.94 per cent purity, has a scleroscope hardness of 13 to 15; cast Zn of the same purity is slightly softer. The effect of small amounts of common impurities is to increase corrosion resistance to solutions, but not in atmosphere. Ordinary Zn is too brittle to roll at ordinary temperatures, but becomes ductile at elevated temperatures; brittleness is thought to be associated with impurities such as Sn.

Zn has a standard electrode potential of +0.761 and is thus electropositive to most structural metals except Al and Mg. This property is the basis of many important uses of Zn, for example, in batteries and electrogalvanizing of steel. Zn is attacked by moist air, CO_2, and SO_2, resulting chiefly in a coating of hydrated basic carbonate of variable composition; some H_2O_2 may be formed in the process. Zn is resistant to attack by dry F_2, Cl_2, and Br_2 but combines rapidly in presence of water vapor. Zn is attacked by acid gases and acids. Zn is an active reducing agent for many ions such as Fe^{+++}, MnO_4^-, and CrO_4^-. Hot caustic solutions form zincates of uncertain composition. Zn vapor reduces CO_2 to CO, the amount depending on the temperature; above 1100°C., the retort temperature of Zn distillation, essentially all CO_2 is reduced to CO, in the presence of excess C. Zn and S will explode when mixed as a powder and warmed. A protective coating of ZnS is formed on masses of Zn by either S or H_2S. When Zn or one of its alloys is burned, melted, or heated to temperatures above 930°F., Zn metal oxide fume of particle diameter 1 μ and below is formed.

4. ***Analytical Determination***

Samples of fumes of Zn, ZnO in air may be collected by means of an impinger, electrostatic precipitator, molecular-membrane filter, or by passing air through a cotton plug moistened with dilute HNO_3. Analysis may be made colorimetrically, using dithizone or di-β-naphthylthiocarbazone, or polarographically.[653]

5. ***Physiological Response***

A brief review by Vallee (6 pages, 28 references) touching on many of the salient features of Zn and its biological significance to man appeared in 1957.[654] Sufficient evidence has accumulated to show that Zn occurs in the body in two different protein combinations: (*a*) as a metalloenzyme in which Zn is an integral part of an important enzyme system, such as carbonic anhydrase for the regulation of CO_2 exchange, and (*b*) as a metal–protein complex in which Zn is loosely bound to a protein, which acts as its carrier and transport mechanism in the body. The possible relation of these Zn–protein combinations in a variety of altered metabolic conditions and diseases is pointed out, and will be discussed in more detail here in the appropriate sections.

Toxicity. Zn salts are astringent, corrosive to the skin, and irritating to the gastrointestinal tract. Because of the last, when ingested they act as emetics. Zn ion, however, is ordinarily too poorly absorbed to induce acute systemic intoxication. After large doses have been ingested, fatal collapse may occur as a result of serious damage to the buccal and gastroenteric mucous membranes. Mass poisonings have been repeatedly recorded[655] from drinking acidic beverages made in galvanized containers; fever, nausea, vomiting, stomach cramps, and diarrhea occurred in 3 to 12 hours following ingestion. The emetic concentration range in water is from 675 to 2280 p.p.m.; the threshold concentration of taste for Zn salts approximates 15 p.p.m.; 30 p.p.m. soluble Zn salts impart a milky appearance to water, and 40 p.p.m., a metallic taste.[656] The lethal dose of Zn ion administered orally to mice is 57 mg./kg.[657] When parenterally administered, Zn depresses the central nervous system, causing tremors and paralysis of the extremities; subcutaneous injection of Zn lactate or valerate in a dose equivalent to 57 mg. of

[653] J. Cholak, D. Hubbard, and R. Burkey, *Ind. Eng. Chem. Anl. Ed.*, **15**, 754 (1943).

[654] B. L. Vallee, *A.M.A. Arch. Ind. Health*, **16**, 147 (1957); *Physiol. Revs.*, **39**, 443 (1959).

[655] G. E. Callender and C. J. Gentkow, *Military Surgeon*, **80**, 67 (1939); J. W. Sale and C. H. Badger, *Ind. Eng. Chem.*, **16**, 164 (1924); *U. S. Natl. Offic. Vital Statist.*, Communicable Diseases Summary, for Sept. 11, 1954.

[656] J. J. Hinman, *J. Am. Water Works Assoc.*, **30**, 484 (1938).

[657] H. Jaeger, *Arch. exptl. Pathol. Pharmakol.*, **159**, 139 (1931).

Zn/kg. killed a cat after 3 days.[657] Orally, soluble Zn salts are more than 100 times less toxic than corresponding salts of Cd, with which Zn is commonly contaminated.

Drinker, Thompson, and Marsh[658] gave from 175 to 1000 mg. of ZnO/day for periods of from 3 to 53 weeks to dogs and cats, and it was tolerated; glycosuria occurred in the dogs, and fibrous degeneration of the pancreas in some of the cats was found at autopsy. No manifest injury occurred in rats from administration of from 0.5 to 34.4 mg. ZnO/day for periods of 1 month to 1 year. Similar lack of response from $ZnCO_3$ is reported. On the other hand, Waltner and Waltner[659] reported that feeding the same salt induced anemia and osteoporosis in rats; 2 per cent metallic Zn in the diet of rats, however, resulted in no injury. Zn acetate fed to rats for 4 months in doses of 10 to 15 mg. daily, and 50 mg. of Zn malate fed to cats for 10 days to 2 months caused no intoxication, according to Salant.[660] Sutton and Nelson[661] found that 0.1 per cent Zn was tolerated in the diet of rats, but that more than 0.5 per cent reduced their capacity to reproduce, and 1 per cent inhibited growth, caused severe anemia, and death. Zn salts in the diet are somewhat more toxic to pigs.[662]

Metabolism. Human intake of Zn is about 10 to 15 mg./day, which is mainly excreted through the intestines. The feces contain about 10 mg. and the urine about 0.4 mg. The normal Zn content of human tissues varies from 10 to 200 μg./g. of fresh tissue. Most organs, including the pancreas, contain around 20 to 30 μg./g.[654] The liver, bone, and voluntary muscle contain from 60 to 180 μg. of Zn/g. of tissue. Exceptionally large amounts are present in the prostate (860 ± 100 μg./g.) and the retina (500 to 1000 μg./g.). The total amount of Zn in the human adult is estimated to be 2 g. No tissue preferentially stores Zn. Whole blood of man contains about 900 μg. per cent of Zn, of which the serum contains from 80 to 160 μg. per cent. Leukocytes contain 3 per cent of total blood Zn. Blood Zn values exhibit no seasonal or diurnal variations nor do they differ between the sexes. Diabetics have normal Zn blood levels.

Only very small amounts of Zn were absorbed and stored in the tissues of dogs, cats, and rats fed Zn compounds for long periods;[658] chief sites of storage were the liver and pancreas. Intravenously injected radioactive Zn^{65} showed that liver, pancreas, and kidney stored large amounts of Zn^{65}, but that the muscular and mucosal layers of the small intestine contained relatively large amounts; more than 50 per cent of the dose was excreted by mice in the feces and 2 per cent in the urine in 170 hours.[663]

[658] K. R. Drinker, P. K. Thompson, and M. Marsh, *Am. J. Physiol.*, **80**, 31, 65 (1927), **81**, 284 (1927).

[659] K. Waltner and K. Waltner, *Arch. exptl. Pathol. Pharmakol.*, **141**, 123 (1929); **146**, 310 (1929).

[660] W. Salant, *J. Ind. Hyg.*, **2**, 72 (1920).

[661] W. R. Sutton and D. E. Nelson, *Proc. Soc. Exptl. Biol. Med.*, **36**, 211 (1937).

[662] R. E. Grimmett, *et al.*, *N. Z. J. Agr.*, **54**, 216 (1937).

[663] G. E. Sheline, I. L. Chaikoff, H. B. Jones, and M. L. Montgomery, *J. Biol. Chem.*, **147**, 409 (1943), **149**, 138 (1943), *J. Exptl. Med.*, **78**, 151 (1943).

Zn is apparently transported in the blood stream as a loosely bound metal globulin complex;[664] blood serum also contains a firmly bound Zn–protein component, which amounts to about 50 per cent of that of the loosely bound fraction.

Ethylenediaminetetraacetate (EDTA) administered to rats intraperitoneally greatly increased the urinary excretion of Zn. Of the various tissues analyzed, only the pancreas and ileum showed a decreased concentration of Zn after EDTA.[665]

Mechanism. Zn is an active component of carbonic anhydrase; removal of Zn results in irreversible inactivation of the enzyme, which is responsible for rapid exchange of CO_2.[654] Zn is also a component of carboxypeptidase that splits terminal amino groups from peptides; 1 atom of Zn is combined to 1 molecule of enzyme. Four dehydrogenases contain Zn that is essential for their action: alcohol dehydrogenase of yeast and liver, lactic acid dehydrogenase, and glutamic dehydrogenase; 2 to 4 moles of Zn are contained per enzyme molecule. Their presence in liver and retina may explain the high concentration of Zn at these sites.

Serum Zn level is lowered in experimental CS_2 poisoning,[666] in pneumonia, bronchitis, erysipelas, in pyelonephritis, and in untreated pernicious anemia.[654]

Industrial Experience. Batchelor, Fehnel, Thomson, and Drinker found no acute or chronic illness in their examination of 24 men who had been exposed to ZnO at levels of 0.3 to 1.64 mg./cu. ft. for from 2 to 35 years.[667] The mean Zn content of the blood of the exposed men was only slightly greater than that of unexposed men. Exposure to mists or fumes of Zn salts may give rise to irritation of the respiratory or the gastrointestinal tracts, but the evidence for these effects is inconclusive. It has been stated that ZnO as dust may block the sebaceous-gland ducts and give rise to a papulopustular eczema in men engaged in packing ZnO in barrels.[668] Sensitivity to ZnO is extremely rare.[669] Unlike ZnO, $ZnCl_2$ has a caustic action, may result in ulceration of the fingers, hands, and forearms of those who use it as a flux in soldering. Affections of the skin have been noted among men handling railway ties impregnated with $ZnCl_2$. Zn stearate has been implicated as a causative agent in pneumoconiosis.[670]

Metal-Fume Fever. Inhalation of fumes of ZnO results in a malaria-like illness with onset some hours after the exposure.[671] Metal-fume fever is not confined to the inhalation of ZnO but may follow exposure to metal fumes of Sb, As, Be, Cd, Co, Cu, Fe, Pb, Mg, Mn, Hg, Ni, and Sn. ZnO fume is a more frequent

[664] I. Vikbladh, *Scand. J. Clin. & Lab. Invest.*, **3,** Suppl. No. 2, 1 (1951).

[665] M. J. Millar, *et al.*, *Nature*, **174,** 881 (1954).

[666] A. E. Cohen and L. D. Scheel, *et al.*, *Am. Ind. Hyg. Assoc. J.*, **20,** 303 (1959).

[667] R. P. Batchelor, J. W. Fehnel, R. M. Thomson, and K. R. Drinker, *J. Ind. Hyg.*, **8,** 322 (1926).

[668] J. A. Turner, *Public Health Repts. U. S.*, **36,** 2727 (1921); J. G. Downing, *J. Ind. Hyg.*, **17,** 147, 150 (1935).

[669] H. E. Freeman, *J. Am. Med. Assoc.*, **119,** 1016 (1942).

[670] U. Uotila and L. Noro, *Folia Med. Naples*, **40,** 245 (1957).

[671] C. C. Sturgis, P. Drinker, and R. M. Thompson, *J. Ind. Hyg.*, **9,** 88 (1927); P. Drinker, R. M. Thompson, and J. L. Finn, *J. Ind. Hyg.*, **9,** 98, 187, 331 (1927); **10,** 13 (1928).

cause, however. The symptoms include chills and fever, which rarely exceeds 102°F., nausea and sometimes vomiting, dryness of the throat, cough, fatigue, yawning, weakness, and aching of the head and body. After a few hours, the victim sweats profusely, and the temperature begins to fall. The condition lasts a day and is never fatal. Occasionally glucose is found in the urine; albuminuria is rare. Mental confusion and convulsions may be present. The vital capacity (lung) may be reduced, a condition which may persist for 15 hours. In 36 of 100 cases observed by Natvig,[672] the condition recurred weekly or more frequently. Leucocytosis (12,000 to 16,000 leucocytes/cu. mm.) persists for 12 hours after the temperature has returned to normal.[671] While the condition persists there is a measure of immunity. Workers are more susceptible on Mondays, and on week-days following a holiday, than on other workdays. A postulated mechanism that seems most reasonable today is that of Lehmann,[673] who suggested that the inhaled Zn-fume particles liberated modified protein from the lung into the blood stream. The subsequent distribution and absorption of the modified protein results in the characteristic response resembling that from the injection of a foreign protein. A recent review of the problem of metal-fume fever from inhaling ZnO, with reports of cases, is given by Rohrs.[674]

6. *Hygienic Standards of Permissible Exposure*

A limit of 15 mg. of Zn/cu. meter air accepted by the American Conference of Governmental Industrial Hygienists was suggested by Drinker, Thomson, and Finn[671] as the maximal concentration that can be inhaled daily without the production of metal-fume fever. In laboratory experiments, a concentration of 45 mg./cu. meter was tolerated for 20 minutes by man.

7. *Flammability*

Powdered Zn presents a hazard of explosion. If stored in damp places, there is danger of spontaneous combustion. Residues from reduction reactions may start a fire if thrown into combustible waste (see also Vol. I, pages 560, 562, 565, 567, 570, and 575).

ZIRCONIUM, Zr

1. *Source and Production*

Zr is associated with other metals in many minerals, but is recovered only from zircon ($ZrO_2 \cdot SiO_2$) and baddeleyite (brazilite) (ZrO_2). Hafnium, Hf, is invariably associated with Zr. Zircon occurs in all igneous rocks but is more common in granite, sylnite (complex silicates), and diorite (alkaline-earth silicates). Zircon is a common constituent of river gravels and beach sands, whence it is

672 H. S. Natvig, *J. Ind. Hyg. Toxicol.*, **19,** 227A (1937) (abstr.).
673 K. B. Lehmann, *Arch. Hyg.*, **72,** 358 (1910).
674 L. C. Rohrs, *A.M.A. Arch. Int. Med.*, **100,** 44 (1957).